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#### Published:

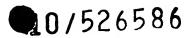
- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 17 June 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: USE OF GRANZYME B AS AN HSP70/HSP70 PEPTIDE DEPENDENT INDUCER OF APOPTOSIS IN TUMOR

(57) Abstract: The present invention relates to a method of inducing or enhancing the expression of granzyme B in natural killer (NK) cells. The present invention relates also to a use of said NK cells for the preparation of a pharmaceutical composition for the ireatment of tumors, viral or bacterial infections or inflammatory diseases. Further, the present invention relates to the use of granzyme B for the treatment of tumors, viral or bacterial infections or inflammatory diseases, wherein the tumor cells or the cells affected by said infection or inflammation express Hsp70 in their cell surface.





# PATENT COOPERATION TREATY C'd PCT/PTO 23 FEB 2005

#### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER See Notification of (Form PCT/ISA/2)	of Transmittal of International Search Report 220) as well as, where applicable, item 5 below.
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/EP 03/09341	22/08/2003	23/08/2002
Applicant		
STEINECKE, peter		
This International Search Report has be according to Article 18. A copy is being t	en prepared by this International Searching Aut ransmitted to the International Bureau.	thority and is transmitted to the applicant
This International Search Report consist  It is also accompanied b	s of a total of sheets. y a copy of each prior art document cited in this	s report.
1. Basis of the report		
<ul> <li>With regard to the language, the language in which it was filed, ut</li> </ul>	e international search was carried out on the ba nless otherwise indicated under this item.	sis of the international application in the
the international search Authority (Rule 23.1(b)).	was carried out on the basis of a translation of t	the international application furnished to this
b. With regard to any nucleotide a was carried out on the basis of the	nd/or amino acid sequence disclosed in the in the sequence listing:	nternational application, the international search
	ional application in written form.	
	ternational application in computer readable for	m.
	to this Authority in written form.	
	to this Authority in computer readble form.	de a catalog to consider the displacement in the
international application	ubsequently furnished written sequence listing of as filed has been furnished.	
x the statement that the in furnished	formation recorded in computer readable form i	is identical to the written sequence listing has been
2. X Certain claims were fo	und unsearchable (See Box I).	
3. Unity of invention is la	cking (see Box II).	
4. With regard to the title,		,
_	submitted by the applicant.	
the text has been establ	ished by this Authority to read as follows:	•
5. With regard to the abstract,	where the development	
the text has been estable	submitted by the applicant. Ished, according to Rule 38.2(b), by this Author ne date of mailing of this international search re	rity as it appears in Box III. The applicant may, port, submit comments to this Authority.
6. The figure of the drawings to be pu		
as suggested by the app		X None of the figures.
because the applicant fa		_
because this figure bette	er characterizes the invention.	

Form PCT/ISA/210 (first sheet) (July 1998)



nal Application No PCT/EP 03/09341

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N5/08 A61K38/48 A61K35/14

According to International Patent Classification (IPC) or to both national classification and IPC

#### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, MEDLINE, BIOSIS, CHEM ABS Data

C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, o	of the relevant passages	Relevant to claim No
X .	WO 99 49881 A (MULTHOFF GABRE 7 October 1999 (1999-10-07) cited in the application page 1, paragraph 1 page 3, paragraph 5 page 8, paragraph 2 page 11, paragraph 2 page 21 -page 26; examples 1-	paragraph 1	12,13, 16,22-24
Х	US 6 261 839 B1 (MULTHOFF GAE 17 July 2001 (2001-07-17) column 1, line 65 -column 2, claims 1,19,20	·	12,13, 16,22-24
X Furth	er documents are listed in the continuation of box C.	χ Patent family members are listed	l in annex.
'Special cat 'A" documer conside E" earlier de filing da 'L" documer which is citation O' documer other m P" documer	nt which may throw doubts on priority claim(s) or s cited to establish the publication date of another or other special reason (as specified) nt referring to an oral disclosure, use, exhibition or	"T" later document published after the In or priority date and not in conflict wit cited to understand the principle or tinvention  "X" document of particular relevance; the cannot be considered novel or cannot involve an inventive step when the decument of particular relevance; the cannot be considered to involve an indocument is combined with one or ments, such combination being obvious the art.  "&" document member of the same paten	ternational filing date h the application but heory underlying the claimed invention of be considered to ocument is taken alone claimed invention nventiove step when the nore other such docu- ous to a person skilled
Date of the a	ctual completion of the international search	Date of mailing of the international se	
7	April 2004	23/04/2004	
lame and m	alling address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL – 2280 HV Rijswijk  Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Authorized officer Sitch, W	



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C.(Continua Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	
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A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; October 2001 (2001-10) MULTHOFF GABRIELE ET AL: "A 14-mer Hsp70 peptide stimulates natural killer (NK) cell activity" Database accession no. PREV200200042332 XP002276403 abstract & CELL STRESS AND CHAPERONES, vol. 6, no. 4, October 2001 (2001-10), pages 337-344, ISSN: 1355-8145	·
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Internal Application No
PC17EP 03/09341

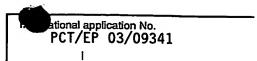
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Category Citation of document, with indication, where appropriate, of the relevant passages  Relevant to claim No.	Category* Citation of document, with indication, where appropriate, of the relevant passages  T DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 17 October 2003 (2003-10-17) GROSS CATHARINA ET AL: "Cell surface-bound heat shock protein 70 (Hsp70) mediates perforin-independent apoptosis by specific binding and uptake of granzyme B." Database accession no. PREV200300583456 XP002276406 abstract & JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 42, 17 October 2003 (2003-10-17), pages 41173-41181,	C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/EP 0	3/09341
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		T	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 17 October 2003 (2003-10-17) GROSS CATHARINA ET AL: "Cell surface-bound heat shock protein 70 (Hsp70) mediates perforin-independent apoptosis by specific binding and uptake of granzyme B." Database accession no. PREV200300583456 XP002276406 abstract & JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 42, 17 October 2003 (2003-10-17), pages 41173-41181,		resevant to claim No.
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Box I Observations where certain claims were found unsearchable (Continuation of Item, 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1, 2, 9-11, 21-24 (all partially), and claims 3, 16-20 (all completely) are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  .
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

on patent family members

Internal Application No
PC17±P 03/09341

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